REMARKS

Applicant wishes to thank the Examiner for the courtesy of a telephone interview on April 18, 2007, wherein the outstanding rejections were discussed. Prior art rejections over Griffais et al and Bennett et al were discussed.

Claims 7, 9-15, 17-20 and 34-44 were pending in the present application. By virtue of this response, claim 36 has been cancelled, claims 7, 12, 15, 20, 34, 35 and 37 have been amended and new claims 45-50 have been added. Accordingly, claims 7, 9-15, 17-20, 34, 35, and 37-50 are currently under consideration. Allowance of the pending claims is respectfully requested.

With respect to all amendments and canceled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and, moreover, has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

The amendments to claims 7, 12, 15, 20, 34, 35 and 37, as well as new claims 45-50, are fully supported by the original application. References to paragraph numbers herein are taken from the instant original application as filed, and not from the published US application. No new matter is added.

No new matter is added by the amendment of claims 7, 12, 15, and 20 to change "substantially complementary" to "100% complementary". Sequences that are "substantially complementary" to a second sequence are understood to include, but not be limited to, sequences that are 100% complementary to the second sequence, as evidenced by lines 3-5 of paragraph [0121], page 41.

Claims 7, 12, 15, and 20 have also been amended to remove the language "from about 8" due to the amendment of these claims to require that the oligonucleotides, antisense RNAs, and/or nucleic acids comprise a sequence that is "100% complementary to SEQ ID NO:5." Since the oligonucleotides, antisense RNAs, and/or nucleic acids in the amended claims comprise a sequence that is 100% complementary to SEQ ID NO:5, the oligonucleotides, antisense RNAs, and/or nucleic acids must comprise the sequence 5'-CTTTGCCTCTAGGGTCCG-3' that is 18 nucleotides/nucleobases in length. Thus, inherently, the oligonucleotides, antisense RNAs, and/or nucleic acids in claims 7, 12, 15, and 20 cannot be less than 18 nucleotides/nucleobases in length. Similarly, the analogous amendments of claims 34 and 35 are also fully supported by the application.

Claim 36 has been cancelled in light of the amendment to claim 7.

Claim 37 has been amended in light of the amendment made to claim 7. Support for this claim is found, e.g., in SEQ ID NO: 8 and SEQ ID NO: 28 and at lines 1-2 of paragraph [0200] and lines 5-6 of paragraph [0206].

New claims 45-50 have been added. Support for these new claims is found, e.g., in paragraphs [0068] and [0129], which clearly indicate that oligonucleotides of the invention may be from about 8 to about 50 nucleotides in length, from 10 to 30 nucleotides, and from 15 to 25 nucleotides. As indicated in paragraph [0020], expressed nucleic acids are alternatively referred to in Applicants' specification as "oligonucleotides."

Information Disclosure Statement

The Examiner asserts that the Information Disclosure Statement (IDS) filed 10/16/06 was in compliance with the provisions of 37 CFR 1.97, but fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document and each non-patent literature publication or that portion which caused it to be listed. The Examiner remarks

that only abstracts of non-patent literature publications CB-CD were provided and CE was missing. Applicants provide herewith full copies of each of references CB, CC, CD and CE. Applicants respectfully assert that the IDS is now fully compliant, including with 37 CFR 1.98(a)(2), and request that the references and information referred to in the IDS be fully considered.

Priority

Applicants thank the Examiner for acknowledging that SEQ ID NO:5 enjoys priority to 5/30/02 and to U.S. Application No. 60/384,228 ("the '228 provisional").

Claim Objections

Claims 42 and 44 are objected to in view of the ordering of dependent claims. The Examiner notes that if the claims are allowed, they will have to be renumbered. Applicants have no objection to the renumbering of the claims once the claims are allowed.

Claim Rejections Under 35 U.S.C. § 112

The Examiner has rejected claims 7, 9-15, 17-20, and 34-44 due to an alleged lack of written description for the previously amended and new claims. With respect to paragraphs [0068] and [0129], to which Applicants previously referred for support for the claim amendments, the Examiner has commented that not all limitations of the amended and new claims are in the paragraphs. Applicants respectfully traverse this rejection.

Applicants contend that the Examiner has not applied the correct standard for adequate written description. Adequate written description under the law does not require that all elements of a claim be contained together within the same single paragraph. Rather, for adequate written description, an applicant's specification must convey with reasonable clarity

to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. *Vas-Cath, Inc. v. Mahurkar*, 935 F. 2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

Furthermore, the Examiner has not met his initial burden of establishing a prima facie case for the rejection by a preponderance of the evidence as to why a person skilled in the art would not recognize in Applicants' disclosure a description of the invention as defined by the claims. The Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257. 265, 191, USPQ at 98 (CCPA 1971). See also Ex parte Sorenson, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987).

Applicants contend that adequate written description for the previously amended and presented claims, as well as the additional new claims added by this amendment, is present in Applicants' specification. Support for the amendment and new claims is found, e.g., in paragraphs [0068] and [0129].

One of ordinary skill in the art would recognize that paragraph [0068] provides *generally applicable* information about the characteristics of the "oligonucleotides" referenced elsewhere in the application, as evidenced by the first sentence of the paragraph which begins, "The term 'oligonucleotide,' as used herein in referring to a nucleic acid of the present invention...." (emphasis added). The sentence at the end of the paragraph indicates that when the term "oligonucleotide" is used elsewhere in the application, that oligonucleotides may, in particular embodiments, be from about 8 to about 50 nucleotides in length, from 10 to 30 nucleotides in length, or from 15 to 25 nucleotides in length. The examiner has provided no justification for limiting the guidance this paragraph provides regarding possible lengths of oligonucleotides only to oligonucleotides found in the same paragraph, rather than extending it more generally to the other oligonucleotides described in the specification.

Similarly, paragraph [0129] likewise indicates some possible ranges in length for the oligonucleotides described elsewhere in the specification. This is evidenced, in part, by the first sentence of the paragraph which begins "The oligonucleotides in accordance with this invention...." The entire paragraph is directed to reciting some selected, alternative possible ranges in nucleotide length for the antisense oligonucleotides described in the specification, making it self-evident that these possible length ranges are intended to apply generally to the antisense oligonucleotides that are the subject of the patent application. Again, the Examiner has no justification for his conclusion that the size ranges of this paragraph which is dedicated entirely to size ranges is somehow not applicable to other oligonucleotides disclosed in Applicants' specification.

Applicants' application clearly indicates that any of the antisense oligonucleotides described in the application, including those directed to oligonucleotides comprising a sequence that is substantially complementary to SEQ ID NO:5, including a sequence 100% complementary or less than 100% complementary to SEQ ID NO:5, may optionally have a length in a range indicated in paragraphs [0068] and [0129].

The Examiner also asserts that if the "oligonucleotide is longer than 18 nucleotides the specification does not disclose what nucleotides can be included to make a nucleotide [*sic*] that is 50 nucleotides long." Applicants, however, contend that contrary to the Examiner's assertions, the present application does provide sufficient guidance as to which nucleotides could be included to make an oligonucleotide that is 50 nucleotides long.

The specification describes antisense oligonucleotides that are substantially complementary to a region of an mRNA encoding mammalian KSR (see, e.g., paragraphs [0014], [0020], [0056], and [0095]). Sequences for both mouse and human KSR are provided in the application. For instance, the specification describes antisense oligonucleotides

comprising a sequence substantially complementary to the CA1 region of KSR (i.e., SEQ ID NO:1), or a portion thereof (see, e.g., paragraphs [0014], [0020], [0056], and [0095]). Sequences for both the mouse and human CA1 region are provided in the application (SEQ ID NOs:1 and 25). SEQ ID NO:5 is one particular target region disclosed within the CA1 region of mouse KSR. (See the mouse KSR coding sequence in Figure 16 in which the CA1 region is labeled near the N-terminus. The portion of the CA1 domain marked with "AS-ODN1 (72-77)" is SEQ ID NO:5.) As noted above, the application further discloses antisense oligonucleotides that are from about 8 to about 50 nucleotides in length. Thus, it will be apparent to one of ordinary skill in the art that Applicants disclose oligonucleotides from about 8 to about 50 nucleotides in length that are complementary to portions of the CA1 region of KSR, or another portion of KSR. As presently claimed, the oligonucleotides must comprise a sequence 100% complementary to SEQ ID NO: 5, but it would be clear to one of ordinary skill in the art that such an oligonucleotide, if it were, for instance, to be 50 nucleotides in length, would not only contain the 18 nucleotides that were 100% complementary to SEQ ID NO: 5, but could also include up to 32 other nucleotides complementary to the nucleotides surrounding SEQ ID NO:5 in a KSR sequence so that the oligonucleotide would be substantially complementary to KSR mRNA.

Applicants further provide a variety of methods for selecting and designing oligonucleotides of up to about 50 nucleotides in length that comprise a sequence 100% complementary to SEQ ID NO:5. Assays for determining which oligonucleotides are substantially complementary to the desired target sequence and/or are suitable for inhibiting expression of KSR are provided. See, e.g., paragraphs [0104], [0106], [0117], [0118], and [0119] of Applicants specification.

In addition, further support for claims 37 and 42 are provided, e.g., in SEQ ID NO: 8 (AS-ODN1 (214-231)) and SEQ ID NO: 28 and at lines 1-2 of paragraph [0200] and lines 5-6

of paragraph [0206]. These are oligonucleotides that are 100% complementary to SEQ ID NO: 5 and meet all limitations of claims 37 and 42.

The Examiner further asserts that if the "nucleotide is shorter than 18, the specification does not disclose what nucleotides can be excluded." Since the claims, as amended, now relate to oligonucleotides, antisense RNAs, and/or nucleic acids that comprise a sequence that is *100%* complementary to SEQ ID NO:5, an 18 nucleotide/nucleobase oligomer, the claims as amended all relate to oligonucleotides, antisense RNAs, and/or nucleic acids that must comprise the sequence 5'-CTTTGCCTCTAGGGTCCG-3' and therefore must be at least 18 nucleotides/nucleobases in length. Accordingly, the Examiner's concerns regarding this issue are moot.

Claim Rejections Under 35 U.S.C. § 102

Rejection of claims 7, 17, 18, and 34-36 over Griffais (WO 99/27105).

Claims 7, 17, 18 and 34-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffais (WO 99/27105). The Examiner asserts that Griffais teaches an oligonucleotide (SEQ ID NO: 20) that is 20 nucleobases and is substantially complementary to SEQ ID NO: 5. To anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Applicant respectfully submits that Griffais et al. does not anticipate claims 7, 17, 18 and 34-36, because the reference fails to disclose or suggest all elements of claims 7, 17, 18 and 34-36. Griffais et al. does <u>not</u> disclose 100% complementary or even any sequences substantially complementary to SEQ ID NO:5. The sequence from Griffais that was cited by the Examiner, 5'-GGACCCAAGAAGCAAAG-3', is neither SEQ ID NO:20 (it actually appears to be part of the 20 mer SEQ ID NO:5583 in the Griffais reference), nor is it substantially complementary to SEQ ID NO:5. As illustrated in the alignment of a fragment of the cited sequence to a fragment of SEQ ID NO:5 that is shown in the Examiner's "sequence search result #9," the cited sequence is partially *identical* to SEQ ID NO:5, not *substantially complementary* to SEQ ID NO:5. More specifically, the sequence cited by the Examiner

appears to contain 15 nucleotides within a 17 nucleotide region that are identical to the non-palindromic SEQ ID NO:5 and therefore cannot be complementary to SEQ ID NO:5. Furthermore, the oligonucleotides, antisense RNAs, or nucleic acids of the claims, as amended, now comprise sequences that are not only substantially complementary to SEQ ID NO:5, but also are 100% complementary to SEQ ID NO:5.

Since Griffais et al. does not teach or suggest each and every element of claims 7, 17, 18, 34 and 35, as amended, Applicant respectfully requests that the rejection of claims 7, 17, 18, 34 and 35 under 35 USC § 102(b) be withdrawn. Claim 36 is canceled, so the rejection of this claim under 35 USC § 102(b) is moot.

Rejection of claims 7, 9-11, 17, 18, 19, 34-36, 38-41 and 43-44 over Bennett et al. (US 6,329,203).

Claims 7, 9-11, 17, 18, 19, 34-36, 38-41 and 43-44 are rejected under 35 U.S.C. 102 (e) as being anticipated by Bennett et al. (U.S. 6,329,203). Bennett is asserted to teach an antisense oligonucleotide that is at least 8 nucleobases (SEQ ID NO: 81) and up to 50 nucleobases and is substantially complementary to SEQ ID NO: 5. As noted above, to anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Applicant respectfully submits that Bennett et al. does not teach or suggest all elements of Applicant's claims, and therefore does not anticipate the claims. The Bennett oligonucleotide SEQ ID NO:81 is directed against (i.e. is complementary to) glioma-associated oncogene-1 and demonstrates 77% inhibition of the non-KSR target sequence, glioma-associated oncogene-1 (Table 1, cols. 45-46). The specification, including at paragraph [0121] page 41, defines "substantially complementary" as when there is "a sufficient degree of complementarity to avoid non-specific binding of the oligonucleotide to non-target sequences". The Bennett et al. sequence is not substantially complementary to SEQ ID NO:5 and does not anticipate the described and claimed antisense oligonucleotides. Applicants have above amended claims 7, 34 and 35 without prejudice to future and further prosecution. The

oligonucleotides, antisense RNAs, and/or nucleic acids of the claims, as amended, now comprise sequences that are 100% complementary to SEQ ID NO:5 and therefore the oligonucleotides, antisense RNAs, and/or nucleic acids must comprise the 18 nucleotide/nucleobase sequence 5'-CTTTGCCTCTAGGGTCCG-3' (i.e., the sequence 100% complementary to SEQ ID NO:5). SEQ ID NO: 81 of Bennett et al. does not comprise this sequence, and therefore does not comprise a sequence that is 100% complementary to SEQ ID NO:5 or meet all elements of the claims.

Accordingly, since Bennett et al. does not teach or suggest each and every element of claims 7, 9-11, 17, 18, 19, 34, 35, 38-41 and 43-44, as amended, Applicant respectfully requests that the rejection of claims 7, 9-11, 17, 18, 19, 34, 35, 38-41 and 43-44 under 35 USC § 102(e) be withdrawn. Claim 36 is canceled, so the rejection of this claim under 35 USC § 102(e) is moot.

Rejection Under 35 U.S.C. § 103

Claims 12-15 and 20: Claims 12-15 and 20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bennett et al. (U.S. 6,329,203) taken with Srivastava (U.S. 6,261,834). Applicant respectfully traverses this rejection.

To establish a prima facie case of obviousness, the prior art references must teach or suggest all the claim limitations. Applicant respectfully submits that claims 12-15 and 20 are not obvious over Bennett et al., in view of Srivastava, since the combination of the two references does not teach or suggest all elements of claims 12-15 and 20. As argued above, Bennett et al. does not teach or suggest all elements of Applicant's claims, particularly as amended. SEQ ID NO:81 of Bennett et al. does not comprise a sequence that is 100% complementary to SEQ ID NO:5. Srivastava teaches a vector comprising an antisense sequence, however, it would not have been obvious nor would one of ordinary skill in the art have been motivated to combine the teachings of Bennett and Srivastava to make or test the

claimed oligonucleotides or vectors comprising DNA comprising the antisense oligonucleotides.

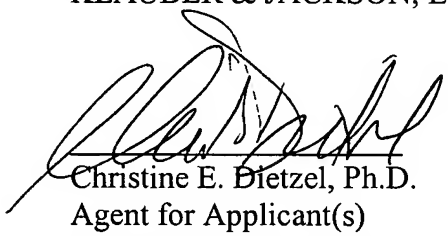
Since Bennett et al., in view of Srivastava, does not teach or suggest each and every element of claims 12-15 and 20 as amended, Applicant respectfully requests that the rejection of claims 12-15 and 20 under 35 USC § 103(a) be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 11-1053** referencing docket no. 1216-1-006CIP. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,
KLAUBER & JACKSON, LLC.



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